Honorable Benjamin H. Settle

UNITED STATES DISTRICT COURT, WESTERN DISTRICT OF WASHINGTON
AT SEATTLE

UNITED STATES OF AMERICA *ex rel.*
(UNDER SEAL)

Plaintiffs,

v.

(UNDER SEAL)

Defendants.

No. C07-0248 BHS

FIRST AMENDED COMPLAINT

FILED IN CAMERA AND UNDER SEAL

PURSUANT TO 31 U.S.C. § 3729 *et seq.*

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

Honorable Benjamin H. Settle

UNITED STATES DISTRICT COURT, WESTERN DISTRICT OF WASHINGTON
AT SEATTLE

UNITED STATES OF AMERICA *ex rel.* MARSHALL S. HORWITZ, M.D.,

AND

THE STATES OF CALIFORNIA, DELAWARE, FLORIDA, HAWAII, ILLINOIS, INDIANA, LOUISIANA, MICHIGAN, MONTANA, NEVADA, NEW HAMPSHIRE, NEW MEXICO, TENNESSEE, and TEXAS *ex rel.* MARSHALL S. HORWITZ, M.D.,

AND

THE COMMONWEALTHS OF MASSACHUSETTS AND VIRGINIA *ex rel.* MARSHALL S. HORWITZ, M.D.,

AND

No. C07-0248 BHS

FIRST AMENDED COMPLAINT FOR VIOLATIONS OF THE FEDERAL FALSE CLAIMS ACT [31 U.S.C. § 3729 *et seq.*]; CALIFORNIA FALSE CLAIMS ACT [CAL. GOVT. CODE § 12650 *et seq.*]; CALIFORNIA PENAL CODE [CAL. PEN. CODE § 550(a)(1), (5), and (6)]; CALIFORNIA INSURANCE CODE [CAL. INS. CODE § 1871.7(b)]; DELAWARE FALSE CLAIMS AND FALSE REPORTING ACT [6 DEL. C. § 1201]; FLORIDA FALSE CLAIMS ACT [FLA. STAT. ANN. § 68.081 *et seq.*]; HAWAII FALSE CLAIMS ACT [HAW. REV. STAT. § 661-21 *et seq.*]; ILLINOIS WHISTLEBLOWER REWARD AND PROTECTION ACT [740 ILL. COMP. STAT. § 175 *et seq.*]; ILLINOIS INSURANCE CLAIMS FRAUD PREVENTION ACT, [740 ILL. COMP. STAT. § 92]; INDIANA FALSE CLAIMS AND WHISTLEBLOWER PROTECTION ACT [IND. CODE ANN. § 5-11-5.5-1, *et seq.*];

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 FIFTH AVENUE, SUITE 2900 • SEATTLE, WA 98101
TELEPHONE (206) 623-7292 • FACSIMILE (206) 623-0594

THE DISTRICT OF COLUMBIA *ex rel.* MARSHALL S. HORWITZ, M.D.,

Plaintiffs,

v.

AMGEN INC.; THE THOMSON CORPORATION; THOMSON HEALTHCARE, INC.; KNOWLEDGEPOINT 360 GROUP, L.L.C.; and DAVID C. DALE,

Defendants.

LOUISIANA MEDICAL ASSISTANCE PROGRAMS INTEGRITY LAW [LA. REV. STAT. § 437 *et seq.*]; MASSACHUSETTS FALSE CLAIMS LAW [MASS GEN LAWS ch.12 § 5 *et seq.*]; MICHIGAN MEDICAID FALSE CLAIMS ACT [MICH. COMP. LAWS. § 400.601, *et seq.*]; MONTANA FALSE CLAIMS ACT [MONT. CODE ANN. § 17-8-401, *et seq.*]; NEVADA FALSE CLAIMS ACT [NEV. REV. STAT. ANN. § 357.010 *et seq.*]; NEW HAMPSHIRE FALSE CLAIMS ACT [N.H. REV. STAT. ANN. § 167.61 *et seq.*]; NEW MEXICO MEDICAID FALSE CLAIMS ACT [N.M. STAT. ANN. § 27-2F-1 *et seq.*]; TENNESSEE MEDICAID FALSE CLAIMS ACT [TENN. CODE ANN. § 71-5-181 *et seq.*]; TEXAS MEDICAID FRAUD PREVENTION LAW [TEX. HUM. RES. CODE ANN. § 36.001 *et seq.*]; VIRGINIA FRAUD AGAINST TAXPAYERS ACT [VA. CODE ANN § 8.01-216.1 *et seq.*]; and DISTRICT OF COLUMBIA PROCUREMENT REFORM AMENDMENT ACT [D.C. CODE ANN. § 1-1188.13 *et seq.*]

FILED IN CAMERA AND UNDER SEAL
(pursuant to 31 U.S.C. § 3730(b)(2))

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 FIFTH AVENUE, SUITE 2900 • SEATTLE, WA 98101
TELEPHONE (206) 623-7292 • FACSIMILE (206) 623-0594

TABLE OF CONTENTS

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

Plaintiff and Relator Marshall S. Horwitz, through his attorneys Hagens Berman Sobol Shapiro LLP, and on behalf of the United States of America, the States of California, Delaware, Florida, Hawaii, Illinois, Indiana, Louisiana, Massachusetts, Michigan, Montana, Nevada, New Hampshire, New Mexico, Tennessee, Texas, the Commonwealths of Massachusetts and Virginia, and the District of Columbia (collectively "the States and the District of Columbia"), and for his First Amended Complaint against defendants Amgen Inc., The Thomson Corporation, Thomson Healthcare, Inc., KnowledgePoint360 Group, L.L.C., and David C. Dale, alleges based upon personal knowledge and relevant documents, as follows.

I. INTRODUCTION

1. This is an action (1) to recover damages and civil penalties on behalf of the United States of America, the States, and the District of Columbia arising from false and/or fraudulent records, statements and claims made, used and caused to be made, used or presented by defendant Amgen Inc. ("Amgen") and/or its agents and employees, The Thomson Corporation, Thomson Healthcare, Inc., KnowledgePoint360 Group, L.L.C. (The Thomson Corporation, Thomson Healthcare, Inc., KnowledgePoint360 Group, L.L.C. are referred to collectively below as the "Thomson Defendants"), and David C. Dale ("Dale") in violation of the Federal Civil False Claims Act, 31 U.S.C. § 3729 *et seq.*, as amended ("the FCA" or "the Act").

2. As set forth below, defendants' acts also constitute violations of the California False Claims Act, Cal. Govt. Code § 12650 *et seq.*; the California Penal Code, CAL. PEN. CODE § 550(a)(1), (5), and (6); the California Insurance Code, CAL. INS. CODE § 1871.7(b); the Delaware False Claims and False Reporting Act, 6 DEL. C. § 1201 *et seq.*; the Florida False Claims Act, FLA. STAT. ANN. § 68.08 *et seq.*; the Hawaii False Claims Act, HAW. REV. STAT. § 661-21 *et seq.*; the Illinois Whistleblower Reward and Protection Act, 740 ILL. COMP. STAT. § 175/1-8; the Illinois Insurance Claims Fraud Prevention Act, 740 ILL. COMP. STAT. § 92; the Indiana False Claims and Whistleblower Protection Act, IND. CODE ANN. § 5-11-5.5-1, *et seq.*; the Louisiana Medical Assistance Program Integrity Law, LA. REV. STAT. § 46:437.1, *et seq.*; the

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 FIFTH AVENUE, SUITE 2900 • SEATTLE, WA 98101
TELEPHONE (206) 623-7292 • FACSIMILE (206) 623-0594

Massachusetts False Claims Law, MASS. GEN. LAWS ch. 12 § 5 *et seq.*; the Michigan Medicaid False Claims Act, MICH. COMP. LAWS. § 400.601, *et seq.*; the Montana False Claims Act, MONT. CODE ANN. § 17-8-401, *et seq.*; the Nevada False Claims Act, NEV. REV. STAT. ANN. § 357.010 *et seq.*; the New Hampshire False Claims Act, N.H. REV. STAT. ANN. § 167:61, *et seq.*; the New Mexico Medicaid False Claims Act, N.M. STAT. ANN. § 27-2F-1, *et seq.*; the Tennessee Medicaid False Claims Act, TENN. CODE ANN. § 71-5-181 *et seq.*; the Texas Medicaid Fraud Prevention Law, TEX. HUM. RES. CODE ANN. § 36.001 *et seq.*; the Virginia Fraud Against Taxpayers Act, VA. CODE ANN. § 8.01-216.1 *et seq.*; and the District of Columbia Procurement Reform Amendment Act, D.C. CODE ANN. § 1-1188.13 *et seq.*

3. Defendants falsely obtained Government reimbursement for Amgen's blockbuster drug Aranesp to treat anemia associated with cancer in patients not receiving chemotherapy. This use is "off-label," *i.e.*, not approved by the Food and Drug Administration ("FDA"), and it in fact has turned out to increase patients' risk of death and injury. Amgen, in collusion with the Thomson Defendants, arranged for the publication of false and misleading articles promoting this use of Aranesp. Defendant Dale allowed Defendants to falsely list him as author of one such article. These articles were then invoked by the Thomson Defendants as a basis for listing Aranesp as indicated to treat cancer patients afflicted by anemia in drug compendia that the Thomson Defendants owned, and these listings formed the basis for Government reimbursement decisions nationwide.

4. Many of the scientific articles at issue were "ghostwritten" by Amgen and the Thomson Defendants. Amgen, the Thomson Defendants, and their agents wrote large portions of many articles that all evidence common authorship, yet the articles appear to be written by different scientists and Amgen's involvement in them remained hidden. In other instances, Amgen used community oncologists who lacked the expertise and resources to manage a drug study as "front" lead authors, while Amgen itself actually managed the study, controlled the results, and dictated the presentation of findings. Those in the medical community would believe

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 FIFTH AVENUE, SUITE 2900 • SEATTLE, WA 98101
TELEPHONE (206) 623-7292 • FACSIMILE (206) 623-0594

the articles were written by prominent and independent physicians, and as such would consider the views of Dr. Dale and the other scientists in deciding a course of treatment. Doctors relying on such articles would be unaware that Dale and the other purported authors were not the true authors – Amgen, the Thomson Defendants, and/or its agents were.

5. If the Government had known that the compendia listings were based on false and misleading science, and that Amgen and the Thomson Defendants had concealed their roles in the articles and the scientific findings, it would not have made reimbursements for Aranesp used to treat anemia of cancer. Furthermore, recent scientific studies have disclosed that Aranesp increases the risk of death and injury to cancer victims not receiving chemotherapy, prompting the FDA to warn physicians against its use. By engaging in this scheme, Defendants risked the lives of patients already struggling to survive cancer. In addition, Amgen was not permitted by federal law to promote off-label uses of its drugs. The Dale article and similar ghostwritten articles promoted the off-label use of Aranesp and other Amgen drugs. By arranging for Amgen and the Thomson Defendants to write the articles for Dr. Dale and others, Amgen and the Thomson Defendants circumvented the law prohibiting a manufacturer from promoting off-label use.

6. As a direct result of defendants' improper practices, federal and state health programs including, but not limited to, Medicare, Medicaid, Medi-Cal, CHAMPUS/TRICARE, CHAMPVA, the Veterans Administration and the Federal Employee Health Benefits Program have been caused to pay false or fraudulent claims for reimbursement for prescriptions of Aranesp and another Amgen blockbuster drug, Neulasta, in populations other than those indicated for treatment – prescriptions that would not have been paid but for the defendants' illegal business practices.

7. The False Claims Act was originally enacted during the Civil War and was substantially amended in 1986. Congress amended the Act to enhance the Government's ability to recover losses sustained as a result of fraud against the United States after finding that fraud in

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

federal programs was pervasive, and that the Act, which Congress characterized as the primary tool for combating government fraud, was in need of modernization. Congress intended that the amendments create incentives for individuals with knowledge of fraud against the Government to disclose the information without fear of reprisals or Government inaction, and to encourage the private bar to commit legal resources to prosecuting fraud on the Government's behalf.

8. The Act provides that any person who knowingly submits, or causes the submission of, a false or fraudulent claim to the U.S. Government for payment or approval is liable for a civil penalty of up to $11,000 for each such claim, plus three times the amount of the damages sustained by the Government. Liability attaches when a defendant knowingly seeks payment, or causes others to seek payment, from the Government that is unwarranted.

9. The Act allows any person having information about a false or fraudulent claim against the Government to bring an action for himself and the Government, and to share in any recovery. The Act requires that the complaint be filed under seal for a minimum of 60 days (without service on the defendant during that time) to allow the Government time to conduct its own investigation and to determine whether to join the suit.

10. Since the passage of the federal False Claims Act, a number of states have passed similar statutes that authorize private persons to file suits to recover damages for false claims presented for payment from state funds. Based on these federal and state provisions, *qui tam* plaintiff seeks through this action to recover damages and civil penalties arising from Amgen's making or causing to be made false or fraudulent records, statements and/or claims in connection with its marketing of its prescription drugs. Defendants knew that their false and fraudulent marketing practices would cause the submission of hundreds of thousands of claims to federal and state health insurance programs for medically unnecessary and potentially harmful prescriptions for Aranesp and Neulasta.

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

II. PARTIES

11. Plaintiff/Relator Marshall S. Horwitz, M.D., Ph.D., is a resident of Washington. Dr. Horwitz at all relevant times was employed by the University of Washington.

12. Dr. Horwitz is a professor of medicine, pathology, and genome sciences at the University of Washington School of Medicine, where he graduated with M.D. and Ph.D. degrees in 1990. Early in his career, he carried out innovative research on the evolution of randomly mutated DNA. More recently, his laboratory has identified genes and molecular mechanisms causing bone marrow failure and cancers of the blood.

13. In 2007, Dr. Horwitz was awarded the prestigious NIH Director's Pioneer Award. As described by the National Institutes of Health ("NIH"), "the NIH Director's Pioneer Award Program is a unique aspect of the NIH Roadmap for Medical Research, a high-risk research initiative of Research Teams of the Future. Pioneer Awards are designed to support individual scientists of exceptional creativity who propose pioneering – and possibly transforming approaches – to major challenges in biomedical and behavioral research. The term 'pioneering' is used to describe highly innovative approaches that have the potential to produce an unusually high impact on a broad area of biomedical or behavioral research, and the term 'award' is used to mean a grant for conducting research, rather than a reward for past achievements. To be considered pioneering, the proposed research must reflect ideas substantially different from those already being pursued in the investigator's laboratory or elsewhere. Biomedical and behavioral research is defined broadly … as encompassing scientific investigations in the biological, behavioral, clinical, social, physical, chemical, computational, engineering, and mathematical sciences."

14. Dr. Horwitz's prior honors include the Presidential Early Career Award for Scientists and Engineers; clinical research scholar awards from the Leukemia & Lymphoma Society, the Doris Duke Charitable Foundation, the Damon Runyon Cancer Research

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

Foundation, and the Burroughs Wellcome Fund; and the University of Washington's Fialkow Scholar Award for outstanding research, teaching, clinical work, and academic citizenship.

15. Dr. Horwitz has direct and independent knowledge of information on which this action is based.

16. Dr. Horwitz and Defendant Dale entered into research collaboration beginning in approximately 1998. The goal of the project was to identify genetic factors causing congenital forms of neutropenia. Congenital neutropenia is a rare disease of children that becomes evident shortly following birth.

17. There are two distinct forms of congenital neutropenia, "cyclic neutropenia" and "severe congenital neutropenia" ("SCN"). In cyclic neutropenia, the patient's neutrophil counts vary in number with a 21-day cycle, such that every three weeks, patients become neutropenic and are vulnerable to infection. In SCN, the patient's neutrophil counts do not vary in number and remain low at all times. Measuring neutrophil counts on a daily basis is often difficult, so it can be challenging for a clinician to correctly determine which form of congenital neutropenia (cyclic neutropenia versus SCN) a patient has.

18. Dr. Horwitz and Dr. Dale succeeded in identifying a gene in which different types of genetic alterations cause the two distinct forms of congenital neutropenia. As a result of their research, for the first time it became possible to use genetic testing to diagnose and discriminate between the two forms of congenital neutropenia.

19. An important distinguishing clinical feature of SCN is that children with SCN, but not those with cyclic neutropenia, frequently develop leukemia.

20. Both forms of congenital neutropenia, cyclic neutropenia and SCN, are usually treated with the Amgen biological agent Neupogen. There is ongoing debate in the research community as to whether treatment with Neupogen causes leukemia in SCN patients. On one side of the debate, there are those who maintain that Neupogen does not contribute to leukemia development; they argue that leukemia is an intrinsic feature of SCN that is unrelated to therapy,

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

because patients with cyclic neutropenia have also been treated with Neupogen and do not appear to have developed leukemia. On the other side of the debate, are those who point out that there are case reports of healthy individuals who have received Neupogen in order to serve as bone marrow transplant donors who have subsequently developed changes in their bone marrow that are consistent with the early stages of leukemia. Because Neupogen is administered frequently to neutropenic cancer patients, the outcome of this debate is important not only for the treatment of a rare hereditary disorder, but it will also have relevance to a large population of patients who receive this drug and for whom long-term risks are not yet known.

21. Dr. Horwitz and Dr. Dale were both authors on two resulting publications that described the outcome of their collaborative research. The second of Dr. Horwitz's and Dr. Dale's collaborative papers was published in the journal *Blood* in 2000 (Dale, D. C., Person, R. E., Bolyard, A. A., Aprikyan, A. G., Bos, C., Bonilla, M. A., Boxer, L. A., Kannourakis, G., Zeidler, C., Welte, K., Benson, K. F., and Horwitz, M. Mutations in the gene encoding neutrophil elastase in congenital and cyclic neutropenia. *Blood*, 96:2317-2322 (2000)). Dr. Horwitz's portion of the research was supported by grants from the United States National Institutes of Health ("NIH"), the Lucille Markey Charitable Trust, the Doris Duke Charitable Foundation, the Leukemia Society of America, the American Cancer Society, the Leukemia Research Foundation, and the National Leukemia Research Association. Dr. Dale's contribution to the research was funded by the NIH and Amgen. Other authors (Mary Ann Bonilla, Laurence A. Boxer, George Kannourakis, Cornelia Zeidler, Karl Welte, and Andrew G. Aprikyan) listed on the paper, who collaborated with Dr. Dale, but with whom Dr. Horwitz did not have a working relationship, received research support and salaries from, and/or served as consultants for, Amgen. Dr. Horwitz had no connections, financial or otherwise, to Amgen.

22. While evaluating the data that was to be included in this paper in *Blood* in 2000, Dr. Horwitz and Dr. Dale determined that one patient who had the diagnosis of cyclic neutropenia appeared to have developed leukemia. If correct, then this observation would

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

significantly contribute to the debate on whether or not Neupogen causes leukemia, because it would conclusively demonstrate for the first time that a patient with a type of neutropenia other than SCN had developed leukemia while being treated with Neupogen.

23. Dr. Dale had expressed considerable consternation over this finding. He stated to Dr. Horwitz that he had been convinced of Neupogen's safety with respect to absence of risk for leukemia when he consulted with Amgen in work that led to Neupogen's approval by the FDA in 1994 for treatment of SCN. However, in his discussions with Dr. Horwitz, Dr. Dale questioned whether Neupogen might not really cause leukemia, after all. Several days after this discussion, Dr. Dale told Dr. Horwitz that he had reviewed the clinical data for the patient and now felt that the patient had been incorrectly given the diagnosis of cyclic neutropenia; Dr. Dale told Dr. Horwitz that he now believed that the patient actually had SCN and that was why the patient had developed leukemia while receiving Neupogen. Dr. Dale explained to Dr. Horwitz that he no longer felt conflicted. Dr. Horwitz did not have access to the clinical data on the patient. (Those data were maintained in an Amgen-funded registry of patients organized by Dr. Dale and the collaborators (also funded by Amgen) with whom he worked.)

24. Also at this time, Dr. Dale and Dr. Aprikyan, a research assistant professor at the University of Washington who worked closely with Dr. Dale, informed Dr. Horwitz that Dr. Aprikyan had repeated the genetic testing on some of the patients whose studies were initially performed in Dr. Horwitz's lab. For a group of several patients, where Dr. Horwitz could not identify genetic alterations, Dr. Aprikyan claimed to have used a more sensitive method for detecting mutations and had found that for some patients with congenital neutropenia whose genetic testing had failed, a diagnosis of SCN could now be made. Dr. Horwitz reviewed Dr. Aprikyan's results, but remained skeptical.

25. When the paper was finally published, with Dr. Dale as the author communicating the final form of the manuscript to the *Blood* journal, the patients in question, including the one

HAGENS BERMAN SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

who had developed leukemia while being treated with Neupogen, had been reassigned to the diagnostic category of SCN.

26. As a result of this encounter, Dr. Horwitz grew suspicious of Dr. Dale's and Dr. Aprikyan's scientific objectivity. Dr. Horwitz specifically felt that Dr. Dale might have been persuaded to reinterpret potentially ambiguous research data in a way that would favor Amgen and minimize risks associated with Neupogen. (Dr. Dale had stated to Dr. Horwitz that he had sent a copy of the preliminary manuscript to Amgen. Dr. Horwitz found this to be unusual and unwarranted, because he was not accustomed to informing funding agencies about work prior to its publication.) Dr. Horwitz also was dissatisfied by the number of authors included on the paper published in the *Blood* journal. Dr. Horwitz could not identify the contributions that they had made to the study, and they were included as authors by Dr. Dale over Dr. Horwitz's objections. As a consequence, Dr. Horwitz grew concerned about Dr. Dale's views on responsible authorship. Similarly, Dr. Horwitz was disappointed with how long it had taken Dr. Dale to prepare the manuscript; what is more, he observed that the writing was not up to the level required by reputable medical journals. Given that Dr. Dale was a prolific contributor to the biomedical literature, it was at this time that Dr. Horwitz first formulated the suspicion that at least some of Dr. Dale's papers might be inappropriately influenced by Amgen, might rely on data of questionable validity, and might involve use of a ghost author.

27. Shortly following publication of this manuscript, Dr. Horwitz and Dr. Dale ended their collaboration. Dr. Horwitz, however, then began to scrutinize papers that Dr. Dale had authored or was to publish soon thereafter.

28. In or about April 2003, Dr. Horwitz reported to the Editor-in-Chief of the journal *Blood* that he had discovered data fabrication in an article prepublished online in that journal. The article is Aprikyan, *et al.*, "Neutrophil elastase mutations in severe congenital neutropenia patients of the original Kostmann family." The lead author of the article was Andrew Aprikyan,

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

Ph.D., and other listed authors included David C. Dale. This paper was supported by a research grant from Amgen.

29. Dr. Horwitz determined that images the authors used to demonstrate their conclusions had been fabricated. Images represented as different in fact were each derived from a common image. In addition, images represented as different were actually composites of separate images that were cut and pasted onto a black background. Dr. Horwitz advised that "it is not surprising that the authors conclude that there is no difference in subcellular distribution between panels C and D, as parts of them derive from the same original image."

30. Based on his analysis, Dr. Horwitz summarized his report to the *Blood* journal editor as follows: "I am concerned that Figure 5 (at least) is the result of a deliberate, crude deception. No matter how this figure was generated, through carelessness or mal intent, it *is* certain that the HL-60 transfection experiments are not reliable. Since they form the experimental basis upon which other major results depend, I believe that it best that the entire paper be retracted." On the basis of Dr. Horwitz's analysis, the *Blood* journal editorially retracted Aprikyan's manuscript. Subsequently, the Office of the Provost of the University of Washington opened an investigation, in conjunction with oversight from the Office of Research Integrity of the Department of Health and Human Services, that continues to this day.

31. Growing increasingly concerned, Dr. Horwitz in a further investigation of Dr. Dale's fraudulent publication practices, reported to Office of the Provost at the University of Washington in or about July 2005 that Dr. Dale had published a paper that strongly suggested plagiarism and involvement of ghost authorship from the pharmaceutical industry. This paper was Dale, D. C., "Distinguished Expert Series: The benefits of haemotopietic growth factors in the management of gynaecological oncology," *Eur. J. Gynaec. Oncol.* 25:133-144 (2004).

32. Dr. Horwitz reported that the Dale article contained unattributed passages that were identical to at least two other scientific papers, one with the lead author named Siena and another with a lead author named Waladkhani. Dr. Horwitz determined that there were at least

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

15 sections where Dr. Dale had used identical or nearly identical words, phrases, sentences, paragraphs, tables, and/or figures as in the Siena article, and at least five sections where Dr. Dale employed identical or nearly identical passages to the Waladkhani article. Figures and tables in the three articles were identical. In addition, the organization of Dr. Dale's paper, especially its second half, paralleled that of the Siena article. These two articles shared 18 common references; the references in both papers were cited in the same ordinal sequence.

33. Dr. Horwitz determined that the Dale and Waladkhani articles discussed areas in which neither of the two lead authors appeared to have expertise. He stated that extensive discussion of the development of pegfilgrastim that was common to both articles suggested a familiarity with biochemistry that seemed to extend beyond the expertise revealed by either of the authors' publication records. Waladkhani, for example, had published a total of just seven papers that were indexed in PubMed. This was his first paper in six years, and he did not appear to ever have worked in the field.

34. Dr. Horwitz reported that all three papers, as well as dozens of other papers by Dr. Dale and like-minded researchers that advocated wider use of Amgen's cykotines, were authored by the same ghost writer from Amgen. He wrote that he believed the ghost author had a master document from which multiple versions were prepared. He believed that the author was the Head of Medical Writing at Amgen, Dr. MaryAnne Foote

35. Dr. Horwitz noted that the ghostwriting practices apparent in the three articles did not comply even with the policy advocated by Dr. Foote, who was the past president of the American Medical Writers Association. He noted that Dr. Foote likely was the actual author of dozens more similar papers as well.

36. Dr. Horwitz reported that Dr. Dale at the time was chair of the American College of Physicians Ethics and Human Rights Committee, which had issued responsible publication practices guidelines decrying ghost authorship. Dr. Dale's actions additionally had violated principles he had proclaimed in a June 25, 1998 lecture for the United States Department of

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

Health and Human Services-mandated Biomedical Research Integrity Video Lecture Series at the University of Washington entitled, "What you should know about plagiarism." Dr. Dale had lectured, "In terms of using someone else's words, where you use their own words, it is always appropriate to use quotation marks around the quoted material or a footnote in some way to indicate the specific source."

37. Defendant Amgen Inc. is a publicly traded company, incorporated in Delaware, with corporate headquarters and its principal place of business in Thousand Oaks, California. With revenues of $12.4 billion in 2005, Amgen is one of the largest pharmaceutical companies in the United States.

38. Defendant The Thomson Corporation ("Thomson") is a Canadian corporation with its principal place of business in Stamford, Connecticut. Thomson is a holding company and, via numerous divisions, does business the world over.

39. Defendant Thomson Healthcare, Inc. ("TME"), an affiliate of Thomson, is a Florida corporation headquartered in Ann Arbor, Michigan. Micromedex, formerly a separate company acquired by Thomson, now is a brand name for products sold by TME. TME, directly or through subsidiaries or affiliates, owns the drug compendia DRUGDEX Information System ("DRUGDEX") and the United States Pharmacopoeia-Drug Information ("USP-DI").

40. Defendant KnowledgePoint360 Group, L.L.C. is a Delaware corporation with its principal place of business in Secaucus, New Jersey. It includes as a division the company formerly named Thomson Gardiner-Caldwell Communications ("TGCC"). KnowledgePoint360 Group is a subsidiary of ABRY Partners, L.L.C. In or about April 2007, ABRY Partners, L.L.C. acquired Thomson Medical Education, which included TGCC. During much of the period relevant to this Complaint, TGCC engaged in a conspiracy to defraud as alleged below. For purposes of this Complaint, KnowledgePoint360 and Thomson Gardiner-Caldwell Communications are referred to collectively as "TGCC."

HAGENS BERMAN SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

41. Defendant David C. Dale. M.D. ("Dale") is a resident of Washington and a physician employed by the University of Washington.

III. JURISDICTION AND VENUE

42. This Court has jurisdiction over the subject matter of this action pursuant to 28 U.S.C. § 1331 and 31 U.S.C. § 3732, the latter of which specifically confers jurisdiction on this Court for actions brought pursuant to 31 U.S.C. §§ 3729 and 3730. In addition, 31 U.S.C. § 3732(b) specifically confers jurisdiction on this Court over the state law claims asserted in this Complaint. Under 31 U.S.C. § 3730(e), there has been no statutorily relevant public disclosure of the "allegations or transactions" in this Complaint.

43. This Court has personal jurisdiction over the Defendants and is a proper venue pursuant to 28 U.S.C. § 1391(b) and 31 U.S.C. § 3732(a) because those sections authorize nationwide service of process and because the Defendants have minimum contacts with the United States. Moreover, the Defendants can be found in, reside, transact, or have transacted business in this District.

44. Venue is proper in this District pursuant to 32 U.S.C. § 3732(a) because the defendants can be found in and transact or have transacted business in this District. At all times relevant to this Complaint, defendants regularly conducted substantial business within this District, and Amgen and the Thomson Defendants made significant sales within the District.

IV. BACKGROUND

A. The FDA Regulatory Scheme

45. Under the Food, Drug, and Cosmetics Act ("FDCA"), 21 U.S.C. §§ 301-97, new pharmaceutical drugs cannot be marketed in the United States unless the sponsor of the drug demonstrates to the satisfaction of the Food and Drug Administration ("FDA") that the drug is safe and effective for each of its intended uses. 21 U.S.C. § 355(a), (d). Approval of the drug by the FDA is the final stage of a multi-year process of study and testing.

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

46. The FDA does not approve a drug for treatment of sickness in general. Instead, a drug is approved for treatment of a specific condition, for which the drug has been tested in patients. The specific approved use is called the "indication" for which the drug may be prescribed. The FDA will specify particular dosages determined to be safe and effective for each indication.

47. The indication and dosages approved by the FDA are set forth in the drug's labeling, the content of which is also reviewed by the FDA. 21 U.S.C. §§ 352, 355(d). An example of the drug's labeling is the printed insert in the drug's packaging. The FDA will only approve the new drug application if the labeling conforms to the uses and dosages that the FDA has approved. 21 U.S.C. § 355(d).

48. Under the Food and Drug Administration Modernization Act of 1997 ("FDAMA"), if a manufacturer wishes to market or promote an approved drug for additional uses – *i.e.*, uses not listed on the approved label – the manufacturer must resubmit the drug for another series of clinical trials similar to those for the initial approval. 21 U.S.C. § 360aaa(b), (c). Until subsequent approval of the new use has been granted, the unapproved use is considered to be "off-label."

49. "Off-label" refers to the use of an approved drug for any purpose, or in any manner, other than what is described in the drug's labeling. Off-label use includes treating a condition not indicated on the label, treating the indicated condition at a different dose or frequency than specified in the label, or treating a different patient population (*e.g.*, treating a child when the drug is approved to treat adults).

50. Although the FDA is responsible for ensuring that a drug is safe and effective for the specific approved indication, the FDA does not regulate the practice of medicine. Once a drug is approved for a particular use, the FDA does not prohibit doctors from prescribing the drug for uses that are different than those approved by the FDA.

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

51. Although physicians may prescribe drugs for off-label usage, the law prohibits drug manufacturers from marketing or promoting a drug for a use that the FDA has not approved. Specifically, under the Food and Drug laws, a manufacturer illegally "misbrands" a drug if the drug's labeling (which includes all marketing and promotional materials relating to the drug) describes intended uses for the drug that have not been approved by the FDA. 21 U.S.C. §§ 331, 352.

52. An off-label use of a drug can cease to be off-label only if the manufacturer submits a supplemental application and demonstrates to the satisfaction of the FDA that the product is safe and effective for the proposed new use. 21 U.S.C. § 360aaa(b), (c).

53. In addition to prohibiting manufacturers from directly marketing and promoting a product's unapproved use, Congress and the FDA have also sought to prevent manufacturers from employing indirect methods to accomplish the same end. For example, FDA regulates two of the most prevalent indirect promotional strategies: (1) manufacturer dissemination of medical and scientific publications concerning the off-label uses of their products; and (2) manufacturer support for Continuing Medical Education ("CME") programs that focus on off-label uses.

54. With regard to the first practice – disseminating written information – the FDAMA only permits a manufacturer to disseminate information regarding off-label usage in response to an "unsolicited request from a health care practitioner." 21 U.S.C. § 360aaa-6. In any other circumstance, a manufacturer is permitted to disseminate information concerning the off-label uses of a drug only after the manufacturer has submitted an application to the FDA seeking approval of the drug for the off-label use; has provided the materials to the FDA prior to dissemination; and the materials themselves must be in an unabridged form and must not be false or misleading. 21 U.S.C. §§ 360aaa(b), (c); 360aaa-l.

55. In sum, the off-label regulatory scheme protects patients and consumers by ensuring that drug companies do not promote drugs for uses other than those found to be safe and effective by an independent, scientific governmental body – the FDA.

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

B. Prescription Drug Reimbursement Under Federal Health Care Programs

1. The Central Role of Drug Compendia in Government Reimbursement

56. The purpose of a drug compendium is to provide a reference for clinicians in which independent professionals review medical literature, select clinically important studies, and summarize and synthesize the information into monographs that inform practitioners' use of drugs in clinical practice. Compendia are intended to contain a summary of scientific evidence about particular drugs and to provide the clinician with selected bibliographic sources if they wish to pursue the topic in greater detail.

57. In January 1989, the predecessor to CMS, the Health Care Financing Administration (HCFA), began developing regulations to implement section 202 of the Medicare Catastrophic Act of 1988, aimed at establishing standards for prescribing outpatient drugs based on accepted medical practice. Congress required HCFA to designate as official those compendia that identified medical practice standards based on published scientific and medical information, provided for a public comment and review process, and provided adequate assurances that the panelists who establish standards were independent from financial or other conflicts of interest. In September 1989, HCFA published in the *Federal Register* its determination that the American Hospital Formulary Service Drug Information ("AHFS DI"), American Medical Association Drug Evaluations ("AMA-DE"), and USP-DI met the selection criteria as official compendia.

58. In 1993, as part of the Omnibus Reconciliation Act of 1993, Congress enacted legislation that authorized government reimbursement for off-label uses of cancer drugs. Under the legislation, Medicare was required to cover an off-label use of a cancer drug if, in general terms, the use was listed in the AHFS DI, AMA-DE, or USP-DI or it was supported by peer-reviewed articles in certain journals outlined by Medicare.

59. In 1995, the United States Pharmacopeia, which at that time published the USP-DI, purchased AMA-DE.

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

60. Originally, Congress listed the same three compendia as authoritative for Medicaid reimbursement purposes, AHFS DI, AMA-DE, or USP-DI. Congress overcame concerns that the compendia would face pressure from the drug industry because all three publishers were controlled by nonprofit associations.

61. In 1997, after the United States Pharmacopeia acquired the AMA-DE, Congress named DRUGDEX as an official reimbursement source. Thomson sought the designation allegedly to gain equal status with competitors. DRUGDEX was never subject to the same rigorous review by Congress and CMS or opportunity for public comment in the *Federal Register* as the other compendia. Instead, it achieved compendial recognition for Medicaid by amendment to unrelated legislation and for Medicare Part D by reference to the Medicaid language.

2. Medicare Part B

62. The Medicare Part B program provides limited coverage for drugs, primarily those that cannot be self-administered and several other narrow categories of medication, including certain anti-cancer drugs.

63. The Medicare Act generally covers "medical and other health services." 42 U.S.C. § 1395k(a)(2). "[M]edical and other health services," in turn, means "services and supplies (including drugs and biologicals which are not usually self-administered by the patient) furnished as an incident to a physician's professional service, or kinds which are commonly furnished in physicians' offices and are commonly either rendered without charge or included in the physicians' bills …." 42 U.S.C. § 1395x(s)(2). The term "drug" also includes "any drugs or biologicals used in an anticancer chemotherapeutic regimen for a medically accepted indication …." 42 U.S.C. § 1395x(t)(2)(A). Though referenced herein at times by the common term "drugs," Aranesp, Neupogen, and Neulasta are biologicals.

64. Medicare Part B will pay for a drug only if the use is "reasonable and necessary" in the circumstances. 42 U.S.C. § 1395y(a); 42 C.F.R. § 411.15(k); Medicare Benefit Policy

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

Manual, Pub. 100-02, Ch. 16, § 20. To determine whether a drug use is "reasonable and necessary," the Medicare rules refer to whether the use is "safe and effective." "Use of the drug or biological must be safe and effective and otherwise reasonable and necessary." Medicare Benefit Policy Manual, Pub. 100-02, Ch. 15, § 50.4.1.

65. Medicare considers a drug use to be "safe and effective" when the use is within the scope of the indications specified on the FDA-approved label. "Drugs or biologicals approved for marketing by the Food and Drug Administration (FDA) are considered safe and effective for purposes of this requirement when used for indications specified on the labeling." Medicare Benefit Policy Manual, Pub. 100-02, Ch. 15, § 50.4.1.

66. In addition, Medicare Part B will cover FDA-approved drugs used for "medically accepted" purposes not indicated on the drugs' approved label in certain circumstances. In general, "FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if the carrier determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice." Medicare Benefit Policy Manual, Pub. 100-02, Ch. 15, § 50.4.2.

67. There are, however, even more specific rules applicable to anticancer chemotherapeutic drugs. Reimbursement for anticancer chemotherapeutic drugs is generally limited to the specific use approved by the FDA and listed on the drug's label. 42 U.S.C. § 1395x(t)(2).

68. However, Medicare will reimburse for an unapproved use of anticancer drugs if (i) the drug is approved, and (ii) the other use is supported by one of three specific compendia set out in the Medicare Act. 42 U.S.C. § 1395x(t)(2)(B). Alternatively, Medicare will reimburse for an off-label use if (i) the drug is approved, and (ii) the Medicare carrier determines that such use is "medically accepted based on supportive clinical evidence in peer-reviewed medical literature

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

appearing in publications which have been identified for purposes of this subclause by the Secretary." *Id.*

69. The three compendia listed in 42 U.S.C. § 1395x(t)(2)(B) as designated to determine reimbursable non-FDA-approved uses of anticancer drugs are, as stated above, the AHFS DI, AMA-DE, and USP-DI. DRUGDEX is not a compendium listed in 42 U.S.C. § 1395x(t)(2)(B) as authoritative for Medicare Part B reimbursement of anticancer drugs.

70. Also separate from Medicare programs qualifying recipients on the basis of age or income is the Medicare End Stage Renal Disease Program, a national health insurance program for people with end stage renal disease. Administration of recombinant forms of human erythropoietin is a mainstay of the treatment of anemia associated with chronic renal failure. In 2005, the End Stage Renal Disease Program covered about 390,000 beneficiaries and spent $2.9 billion for medications. Recombinant forms of erythropoietin accounted for more than $2 billion of this spending and erythropoietin was the highest-expenditure drug in all of Medicare Part B.

3. Medicaid

71. Whether an FDA approved drug is listed for a particular indication (*i.e.*, use) determines whether a prescription for that use may be reimbursed under Medicaid and other federal health care programs.

72. Medicaid is a public assistance program providing for payment of medical expenses for low-income patients. Funding for Medicaid is shared between the federal government and state governments. The Medicaid program subsidizes the purchase of more prescription drugs than any other program in the United States.

73. Although Medicaid is administered on a state-by-state basis, the state programs adhere to federal guidelines. Federal statutes and regulations restrict the drugs and drug uses that the federal government will pay for through its funding of state Medicaid programs. Federal reimbursement for prescription drugs under the Medicaid program is limited to "covered

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

outpatient drugs." 42 U.S.C. § 1396b(l)(10), 1396r-8(k)(2), (3). Covered outpatient drugs are drugs that are used for "a medically accepted indication." 42 U.S.C. § 1396r-8(k)(3).

74. A medically accepted indication, in turn, is a use which is listed in the labeling approved by the FDA, or which is included in one of the drug compendia identified in the Medicaid statute. *Id.* § 1396r-8(k)(6). As stated above, these three compendia are the AHFS DI, USP-DI, and DRUGDEX.

4. Medicare Part D

75. Starting in January 2006, Part D of the Medicare Program provided subsidized drug coverage for all beneficiaries. Low income individuals will receive the greatest subsidies. Aranesp and Neulasta will be utilized by Part D beneficiaries.

The Medicare Part D program adopts the coverage criteria used in the Medicaid statute. *See* 42 C.F.R. § 423.100 (referencing the definition of "medically accepted indication" in the Medicaid statute). Consequently, it only covers a drug if it is used for a FDA-approved use or is supported by citation in one of the compendia relied upon by the Medicaid program, the AHFS DI, USP-DI, and DRUGDEX.

5. Reimbursement under other federal health care programs

76. In addition to Medicaid and Medicare, the federal government reimburses a portion of the cost of prescription drugs under several other federal health care programs, including but not limited to CHAMPUS/TRICARE, CHAMPVA and the Federal Employees Health Benefit Program.

77. CHAMPUS/TRICARE, administered by the United States Department of Defense, is a health care program for individuals and dependents affiliated with the armed forces. CHAMPVA, administered by the United States Department of Veterans Affairs, is a health care program for the families of veterans with 100 percent service-connected disability. The Federal Employee Health Benefit Program, administered by the United States Office of Personnel Management, provides health insurance for federal employees, retirees, and survivors. Coverage

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

of off-label drug use under these programs is similar to coverage under the Medicaid program. *See, e.g.*, TRICARE Policy Manual 6010.47-M, Ch. 7, Sec. 7.1 (B) (2) (March 15,2002); CHAMPVA Policy Manual, Ch. 2, Sec. 22.1, Art. II (A)(2) (June 6, 2002).

78. During the time period relevant to this Complaint, the off-label uses of Aranesp and Neulasta promoted by Amgen were not eligible for reimbursement under any of the various federal health care programs.

6. Direct purchases by federal agencies

79. In addition to reimbursing drug purchases through Medicare, Medicaid, and other federal health care programs, the United States is a significant direct purchaser of prescription drugs through various federal programs. Defendant's illegal and misleading off-label promotion of Aranesp and Neulasta has resulted in increased purchases of these drugs by these programs, including, but not limited, to the following.

a. Programs administered by the Department of Veterans Affairs

80. The Department of Veteran Affairs ("VA") maintains a system of medical facilities from which all pharmaceutical supplies, including prescription drugs, are dispensed to beneficiaries. It also supports a mail service prescription program as part of the outpatient drug benefit. The system serves approximately four million veterans. The VA directly purchases prescription drugs, including Aranesp and Neulasta, that are dispensed through these facilities and programs.

b. Programs by the Department of Defense

81. The Department of Defense ("DOD") provides prescription drug coverage to approximately eight million active duty personnel, retirees, and their families through three points of service: military treatment facility outpatient pharmacies, TRICARE managed care contractor retail pharmacies, and the National Mail Order Pharmacy Program. DOD negotiates independent contracts to purchase the majority of the prescription drugs, including Aranesp and Neulasta, provided through these programs.

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

C. The FDA-Approved Indications for Aranesp, Neupogen, and Neulasta

82. **Aranesp.** Introduced in 2001, Aranesp (darbepoetin alfa) is approved in the United States, most countries in Europe, Canada, Australia, and New Zealand for the treatment of anemia associated with chronic renal failure in patients both on dialysis and not on dialysis. In 2002, Aranesp was also approved in the United States and Europe for the treatment of chemotherapy-related anemia. Aranesp is a recombinant erythropoietic protein that stimulates production of oxygen-carrying red blood cells, with greater biological activity and a longer half-life than Epoetin alfa.

83. **Neupogen.** Neupogen (filgrastim), launched in 1991 in the U.S. and Europe, is a recombinant version of a human protein that selectively stimulates the production of infection-fighting white blood cells, called neutrophils. It is indicated to decrease the incidence of infection as manifested by febrile neutropenia in patients with non-myeloid malignancies receiving myelo-suppressive anti-cancer drugs.

84. **Neulasta**. Neulasta (pegfilgrastim) received approval in 2002 in the United States and Europe for reducing the incidence of infection from chemotherapy-induced neutropenia in cancer patients with non-myeloid malignancies. Neulasta, a longer-acting form of filgrastim than Neupogen, has been shown to decrease the incidence of infection as a result of chemotherapy-induced neutropenia with a once-per-cycle injection.

85. Three erythropoietic drugs are currently approved for certain indications for the treatment of anemia in the United States: recombinant erythropoietin alfa (Epogen and Procrit) and darbepoetin alfa (Aranesp). Two drugs with selective granulocyte colony stimulating factor activity, filgrastim (Neupogen) and pegfilgrastim (Neulasta), are currently approved in the United States for certain indications for the treatment of neutropenia. Although Epogen, Procrit, and Aranesp compete with one another, as do Neupogen and Neulasta, all five are manufactured by Amgen. Of this class of blood cell growth factors, Epogen, Procrit, and Neupogen are considered "first generation" drugs. Epogen and Procrit were first approved by the FDA in

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

1993. Neupogen, as noted above, was first approved in 1991. Each of these first generation drugs are each covered by multiple patents, which are expected to expire over a timeframe extending from 2006 to 2011. "Second generation" glycosylation variants of these drugs have been more recently introduced; as indicated above, Aranesp was approved by the FDA in 2001 and Neulasta in 2002. Aranesp and Neulasta have extended patent protection and will be competing with other manufacturers' "biogeneric" versions of recombinant erythropoietin alfa and filgrastim, respectively, once patents protecting Amgen's first generation of drugs have fully expired.

86. Total U.S. sales for Aranesp in 2005 were $2.1 billion and for Neulasta $1.9 billion. In the first nine months of 2006, U.S. sales of Aranesp were $2.03 billion and for Neulasta $1.63 billion.

87. Anemia, for which Aranesp is used, is a condition that occurs when the blood does not contain enough red blood cells.

88. Red blood cells carry oxygen from the lungs to the body's tissues. In a healthy person, the body sends signals to the bone marrow to create more red blood cells whenever the body needs more oxygen. A hormone called erythropoietin, produced in the kidney, is the signal that stimulates the bone marrow to produce red blood cells. When the body does not produce enough erythropoietin, fewer red blood cells are produced, and therefore less oxygen is delivered to the body.

89. Certain diseases – such as cancer and chronic kidney disease – are related to anemia. Cancer patients undergoing chemotherapy often suffer from anemia because chemotherapy attacks not only cancerous cells, but other cells in the body as well, including red blood cells. In kidney disease patients, kidney function is reduced. Erythropoetin, the body's signal that tells bone marrow to make more red blood cells, comes from the kidneys, so in these patients, fewer red blood cells are produced.

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

90. Some common symptoms of anemia include: fatigue, weakness, rapid heartbeat, shortness of breath, dizziness or fainting, feeling cold, sadness or depression, and shortness of breath. Anemia can strain the heart as it overworks to deliver oxygen throughout the body. It also can make certain cancer therapies less effective and can interrupt chemotherapy treatment. If left untreated, anemia can result in the need for red blood cells transfusions.

91. In some cases, blood disorders are related to other diseases and conditions. Chronic diseases like kidney disease can affect the production of erythropoietin, an important glycoprotein that stimulates the production of red blood cells. An inadequate number of red blood cells reduces the amount of oxygen delivered throughout the body and can represent a serious complication to patients of chronic illness.

92. In cancer patients, chemotherapy can cause blood disorders. Chemotherapy – the use of drugs to treat cancer – works by seeking and attacking fast-growing cells. In addition to attacking cancerous cells, chemotherapy also kills normal cells, including a certain type of white blood cell called neutrophils, which help the body fight infection. About half of the 1.6 million chemotherapy patients in the United States are at risk for developing lower than normal white blood cell counts – a condition called neutropenia. This places them at potential risk for infection and can postpone chemotherapy treatments. Neutropania is the condition that Neulasta is prescribed for.

V. THE DEFENDANTS' FRAUDULENT SCHEME

A. Amgen and Thomson Conspired to Obtain Government Reimbursement of Aranesp for Anemia of Cancer Based On False and Misleading Science

93. Amgen and the Thomson Defendants conspired to ghostwrite scientific articles that promoted the use of Aranesp for anemia of cancer based on false and misleading science. In addition, Amgen used community oncologists as "front" lead authors to publish articles that promoted the off-label and dangerous use of Aranesp based on false and misleading science, without disclosing Amgen's central role in organizing and managing the studies and determining

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

the findings. Amgen and the Thomson Defendants used certain of these tainted studies, including the Smith study and Charu abstract described below, as the basis for listing Aranesp in Thomson-owned drug compendia as indicated to treat anemia of cancer, and these compendia listings were then used by the Government as the basis for reimbursement decisions. If the Government had known of the fraudulent origin of the compendia listings and the true danger of this use of Aranesp, it would not have provided such reimbursement.

1. Amgen and Thomson conspired to ghostwrite articles in medical journals that falsified scientific studies

a. The fraudulent practice of ghostwriting

94. The integrity of the published record of scientific research depends not only on the validity of the science but also on honesty in authorship. Editors and readers need to be confident that authors have undertaken the work described and have ensured that the manuscript accurately reflects their work, irrespective of whether they took the lead in writing or sought assistance from a medical writer. The scientific record is distorted if the primary purpose of an article is to persuade readers in favor of a special interest, rather than to inform and educate, and this purpose is concealed.

95. Ghost authorship exists when someone has made substantial contributions to writing a manuscript and this role is not mentioned in the manuscript itself.

96. The World Association of Medical Editors ("WAME") is a community of 1170 medical editors of 733 journals who work together to facilitate cooperation and communication among editors of medical journals throughout the world. Members work to improve editorial standards and promote professionalism in medical editing through education, self-criticism, and self-governance.

97. WAME considers ghost authorship dishonest and unacceptable. Ghost authors generally work on behalf of companies, or agents acting for those companies, with a commercial interest in the topic, and this compounds the problem. For example, a writer employed by a

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594

commercial company may prepare an article and then invite an expert in the field to submit the work, perhaps with minor revisions, under his or her own name. The submitting author may be paid, directly or indirectly, for this service. In other circumstances, investigators may pay a professional writer to help them prepare for their article but not mention this assistance, gaining credit for writing they have not done. Although editors of publications often seek to avoid publication of ghostwritten articles, these articles are often very difficult to detect.

98. Submitting authors bear primary responsibility for naming all contributors to manuscripts and describing their contributions. Ghost authorship would be avoided if corresponding authors listed everyone else who participated in the work, including those who contributed only to the writing, along with their individual contributions and institutional affiliations, stated explicitly how the work was paid for, and fully disclosed any further potential competing interests.

99. However, responsibility for ghostwritten manuscripts goes beyond individual authors. Other parties, including companies – such as marketing, communications, and medical education companies who are paid to assist pharmaceutical and medical device companies in disseminating favorable messages about their products – may initiate the sequence of events for which the author is the final and most easily identified participant.

100. Various participants in the medical field have incentives to ghostwrite articles.

101. Academicians often wish to have as many publications associated with their names as possible. This may help in obtaining additional grants, promotions and consulting contracts.

102. Pharmaceutical companies also have motives for promoting such articles. An article written about these drugs lend the appearance of impartiality. If these articles promote off-label use they allow the company to remain hidden while promoting such use in an effort to avoid a violation of federal law.

HAGENS BERMAN
SOBOL SHAPIRO LLP
1301 Fifth Avenue, Suite 2900 • Seattle, WA 98101
Telephone (206) 623-7292 • Facsimile (206) 623-0594